by external factors such as stress, sunburn, trauma, other infections, etc. Applicant is not claiming to kill the virus, but merely to inactivate the virus and prevent lesion formation. The stage of the disease when a precursor symptom or lesion starts to occur is immaterial to the effective suppression and inactivation of the virus attack in accordance with applicant's invention. It makes no difference whether the original Herpes infection was one year or five years old before the outbreak of the symptoms being treated. Applicant's treatment regimen is the same, namely reverse the virus attack by upsetting the viral ionized state, restoring the attacked cell electrical state to balanced normal, and driving the virus back to the ganglia and its dormant state. As shown by the results in Table 1.1 when the very preliminary initial symptoms of the development of a lesion occurred and the low voltage was immediately applied in accordance with the present invention, the development of lesions was inhibited, and in most cases, actually stopped. By ignoring the stage of the disease from onset in the patient, applicant has been able to demonstrate that the application of the low voltage to the lesion site actually can reverse or at least limit the development of the lesion and force the rejection of the virus by the cell under attack. The fact that some cells can resist the viral attack while others cannot, clearly indicates that there is something missing in certain cells that are subject to attack. Applicant believes that it is a deficiency in the electrical state of the cell that makes it subject to attack. By applying the external stimulation as near as possible to the cell that is being attacked, applicant is able to assist the cell

back to normal electrical balance and to throw off the attack and to prevent the formation of the lesion. This process is described in complete detail on pages 8-11 of the specification.

It is respectfully submitted that the procedure followed by applicant does not assume identical lesion development for each subject, but rather sets forth as the preferred treatment mode application of the low voltage electrical current to the site of the developing lesion usually indicated by a tingling or itching before the development of the lesion. It has been found, however, that if immediate application is neglected or not undertaken, even after the lesion develops, direct application at the site hastens the healing of the lesions by what applicant believes is the same process as the prevention of the development, namely the assisting of the cell to reject the attack of the virus and to restore the cell to its normal balanced electrical state. The application of the electrical stimulation at the site of the interaction of the virus and a susceptible cell appears to reinforce the natural defenses of the cell and to help it to reject the attack by the viral nucleocapsid and to cause the virus to remain in the enveloped virion. Granted, this encapsulated virus may again become active in the host and attack some other set of cells when again stimulated. These subsequent symptoms, however, can be the subject of further electrical stimulation to prevent development of lesions at that time.

The basic electrical/biological mechanism by which this action is accomplished is indicated on pages 8-10 of the specification. This mechanism is also described in the references

cited in the specification and in the bibliography in more detail. Copies of the cited references can be furnished, as well as the applicant can be made available for an interview to further explain in detail the specific action set forth in the specification that is believed to take place upon the application of the electrical stimulation claimed by applicant.

It is believed that the development of the virus and its attack upon the healthy cells as described in pages 6-10 is currently a generally accepted explanation of what happens upon infection of the human body with a virus of the Herpes type. (see the cited references). Applicant has discovered that the application of the low voltage, low current electrical stimulation at the site of the viral attack acts directly through the electrical control system of the body to deactivate the viral attack and to reinforce and strengthen the cell to return to its normal state. Without a "susceptible cell" to attack, the virus is forced to retreat back to the dorsal root ganglia where it remains dormant until again triggered into action.

Concerning the Examiner's reference to Diethelm's apparatus as providing "a means for accelerating the healing of the Herpes Simplex", applicant does not dispute that Diethelm may get some beneficial effect by applying an AC voltage to the dermatomes of the nervous system because the electrical stimulation of the dermatome will cause the neuromuscular system to regulate to normal electrical state and the injury will therefore heal faster because the neurosystem is in the normal state and not in a trauma state. Diethelm may very well see some healing of the lesions after

application of his AC to the dermatome controlling the site of the lesion. Applicant respectfully submits, however, that this is not the same as applicant's invention wherein applicant "treats" the virus at the cell level, directly at the site of the lesion development. All of the claims require application of the DC directly to the skin at the virus attack site.

The structure of the herpes virus is described in detail in pages 3 and 4 and the mechanism by which it appears to attack healthy cells is further detailed on pages 5 and 6 of the specification. This, it is believed, is standard "textbook" molecular cell biology and is described in some detail also in chapter 5 of the book entitled "Molecular Cell Biology" by James Darnell, Harvey Lodish and David Baltimore, published by Scientific American Books copyrighted in 1990. Pages 179 and 180 describe the virus maturation cycle and its effect on infected host cells in a manner very similar to that set forth in the specification.

The change in cell capacitance due to application of an electric field or current is described in detail in the references cited on page 14 of the specification, particularly Cheng. The enclosed exhibit A is a summary of the theoretical working of the micro-amperage current in the cell structure as reported by Cheng and others. It is extracted from a report on a study entitled "Theoretical Basis of Bioelectric Interfacing using Micro-amperage Current" done by applicant and Robert B. Webster at the University of California, San Diego Industrial Medical Center. Exhibit A is merely included here as another explanation of the current state of the art relative to cell electrical states.

211

Applicant respectfully submits the specification which is based on the published results of others cited in the bibliography provides sufficient basis to overcome the rejection of the specification under 35 USC Sec. 112, first paragraph as incomplete. It is settled textbook microbiology that individual cells have a balanced electrical state that can be upset by chemical, trauma, pathological, and/or electrical events. Viral infection of a cell upsets the electrical balance of the cell. Applicant restores that balance as clearly set forth in the specification and claims. For the same reasons applicant believes that the rejection of the specification under 35 USC Sec. 101 should also be withdrawn. If the citations referenced by the applicant are not readily available to the Examiner, applicant would be pleased to supply representative copies to show the state of the art upon which applicant bases his invention.

Applicant has rewritten claims 12 and 18 as 27 and 28 to define only the steps actually taken to produce the results described in the specification. It is believed the specification and the clinical results recited clearly support claims 27 and 28 which are directed to the inhibiting of the development of herpetic lesions and the treatment of herpetic lesions, respectively. The claims are written without language directed to the change in electrical state of the cell, as applicant believes happens, but rather only to the specific steps of applying the DC electrical voltage and the control and frequency of application which produces the desired results. It is respectfully submitted that neither Diethelm nor any of the other art cited or known to applicant teach

512

the specific regimen of treatment detailed in claims 27 and 28 and the dependent claims thereon. Diethelm teaches a separate and distinct method of treatment for Herpes virus. Diethelm uses a pulsed DC voltage and current applied to the dermatomes of the nervous system of the body. Applicant's method is directly opposite in that a constant DC is applied directly to the cells under attack at the location on the body where the lesion symptoms are occurring and where the lesions ultimately develop if untreated.

The Examiner's indication that the Diethelm "biological mechanism could be similar to applicant's since both devices use DC current applied to the inflicted area" is respectfully traversed. As pointed out above, applicant uses a very low wattage, low current constant DC voltage applied directly to the cell under attack by the virus. Diethelm, on the other hand, uses a pulsed DC which actually, in applicant's view, is an AC field applied to the dermatome within which the afflicted cells are located. There is no teaching whatever by Diethelm of direct treatment of the cells under attack, but rather an attempt to alleviate the trauma state i.e., the pain from the cells in which the lesions have occurred. There is no teaching by Diethelm of the treatment of the precursor symptoms. Also, the Diethelm treatment indicates a much higher level of current applied over longer periods of time at much greater intervals than taught by applicant. Applicant believes that applicant's regimen as set forth in the claims and described in detail in the specification produces an action that not only prevents development of lesions in most cases, if started promptly

after precursor symptoms, but also causes the developed lesions to subside much more rapidly than with a Tens unit, such as Diethelm. While applicant states the output can be a maximum of 30 milliamps, in most cases it is more like microamps because of the resistance of the skin and the cells involved in the treatment. As set forth in Diethelm, column 3, lines 29-45, it is seen that Diethelm prefers a frequency of 30 hertz for the "pulsed DC". This, it is submitted is an AC compared to applicant's invention. Also the treatment periods as indicated in col. 4, lines 5-8 are preferred to be about 20 minutes each, and repeated at about five hour intervals over a period of five days or so. It can be seen from this that the concept patented by Diethelm is totally different from the concept proposed by applicant and that the treatment mechanism obviously is different, although the end result in some cases may be similar.

While applicant firmly believes that the mechanisms described in the specification as to the electrical effect of the application of the DC voltage to the cells in the skin is what happens, claims 27 and 28 and the dependent claims thereon as now rewritten are directed to the method of treatment, irrespective of what the actual cellular electrical state mechanism may be. It is believed these claims are patentable over Diethelm, and the other art known to applicant.

Claim 4, and dependent claims 6, 10 and 11 are directed to the electrochemical effect on the cell structure by the application of a low voltage DC current.

In view of the foregoing discussion of the state of the art and textbook microbiology, it is respectfully submitted claim 4 is fully supported by the specification. Further, neither Diethelm nor any other art known to applicant shows or suggests the steps of applicant's claim 4.

Claim 29 adds details of the treatment regimen recited in claim 4. Claim 30 is directed to the repeated stimulating of the mitochondrial function of both healthy and virus infected cells to throw off the virus attack and cause the virus to retreat to the ganglia.

In view of the foregoing amendments and remarks, reconsideration and allowance are earnestly solicited.

In the event the Examiner believes that contact with applicant's attorney would be advantageous toward the disposition of this case, he is herein requested to call applicant's attorney at the phone number noted below.

Respectfully submitted

WALL and ROEHRIG

By Robert O. Wright
Robert O. Wright
Reg. No. 17,097

ROW/pp
Hills Building - 7th Floor
Syracuse, NY 13202
(315)422-7383

215

platelets to aggregate and adhere to walls of blood vessels near damaged sites, which is the initiation of blood clotting and plugging leakes in blood vessels.[31]

Micro-amperage Current

The principle of micro-amperage (uA) (millionth of an ampere) current as a treatment modality is to interface an electronic circuit with the damaged tissue to build up the capacitive state and return the cell back to homeostasis. The theory is similar to recharging a battery.

> Electrical current perfused through tissues creates a force on electrically charged ions present at interfaces between different types of tissues and in cell membranes. Conduction of current through the tissues depends on ionic movement. When electrical currents are introduced into the body, ions accumulate at tissue interfaces and at cell membranes, creating a charge that is opposite to the charge of the voltage applied at the electrodes. The potential difference that occurs between each electrode and the tissue is created by electrolytic polarization. This phenomenon...occurs in living tissue, which is comparable to a conductor with capacitance.[32]

The muscle tissue and nerves are excellent natural conductors of the body; abundant ions and electrolytes are enclosed within a lipid, non-conductive, insulating membrane. The electrons in the completed circuit will follow a path of least resistance,[33] so the current will flow lengthwise through the muscle or nerve with less resistance than through the surrounding medium. Nerves conduct current six times

better that of muscle tissue while muscle conducts four times better lengthwise (along myofibrils) than transversly.[34] As an electrical current travels through the tissues (given it is of high enough amperage) it will enervate the larger, myelinated nerve fibers before the smaller, un-myelinated nerves as the threshold of excitability becomes lower as fiber diameter increases.[35] This has significance in controlling pain according to the Gate Theory by Wall and Melzack.

uA current has been shown to speed wound healing of soft tissue injuries 150% to 250% above normal healing rates.[36,37] There are also immediate increases in range of motion (ROM), muscle strength, release of muscle knots and rapid reduction in edema and inflammation as well as long term pain relief.[38] uA current has been shown to be compatible with the bodies own electrical signal, thus it amplifies the bodies own healing parameters.[39]

A difference must be understood between uA and mA (thousandth of an ampere) current. uA current is a minute electrical signal, while mA current is high enough amperage to cause muscular contraction. mA electrical stimulation is a well used physical therapy modality as a substitute for exercise until an injured joint may be moved without major risk of re-injury. This is to increase the biochemical/ metabolic pathways that speed the healing parameters by

muscle enervation during stasis. This includes building up glycolytic enzymes, increasing ATPase activity, increasing glycogen stores, changing metabolic characteristics and changes of muscle tissue types from fast to slow twitch fibers.[40,41]

Cellular Effects

uA current, working on a different principle of healing, actually recharges the energy level of the cell which changes the biochemical working of the cell at micro levels. This has been shown to increase ATP energy production by up to 500% and increase protein absorption into the cell between 30-40%.[42,43,44,45] There is debate on whether this is a separate mechanism due to electrical stimuli or a secondary effect of the cell as a response to increased energy. Just as an ideal parameter is stated by researchers, other reports show the negative effects of higher uA current.[46,47] Currents above 1000 uA were shown by Cheng to decrease ATP production below that of the no stimulation (control) group as well as decrease protein metabolism and amino acid transport.[48] Enkephalins and endorphins are released (terminate the pain signals from nociceptive receptors by inhibiting the interneurons),[49] as well as histamine and prostaglandin resolution at the injury site.[50]

Cellular Capacitance

Ngok Cheng[68] has shown that the major mechanism to tissue repair due to uA electrical currents is the generation of ATP and an increase of protein synthesis. This is done not by DNA initiating activity but by changes in ionic concentrations within the cell. Mitchell's Chemiosmotic Theory[69] states that

movement of protons down their concentration gradients is coupled to the synthesis of ATP. As shown earlier the cell has a gradient formed by unequal distribution of ions which also results in a electrical gradient. This is collectively called the electrochemical gradient. "Much evidence shows that in mitochondria... the synthesis of ATP from ADP + P_i occurs *only* via the electrochemical proton gradient across the inner mitochondrial membrane."[70]

The mitochondria is a self contained organelle within the cell that has its own potential gradient respective to the interior of the cell and its own interior. The higher the capacitance of the cell means an analogous increase in potential difference for the mitochondria[71] and hence, an increase in its function. Cheng shows it to be possible to increase the potential of the cell by electrical interfacing (a connection between an electrical circuit and a physiological membrane):

> During electrostimulation, the electrons react with water molecules at the cathode side to produce hydroxyl ions, while at the anode side protons are formed. Thus, between the anode and cathode interface, a proton gradient and a potential gradient across the tissue and the medium are created. Hence protons under the influence of the electric field and the concentration difference should move from anode to cathode. Since the rate of proton formation at the anodic interface is equal to the rate of proton consumption at the cathodic interface, the net pH of the system, medium and tissue, remains undisturbed. As the migrating protons reach the mitochondrial membrane-bound ATPase, ATP will be formed.[72]

Thus, when "we discuss the current 'passing through' the membrane capacitance [author's term], the changes haven't physically penetrated the membrane itself, the current can pass through the membrane even though ions cannot."[73] An so, by increasing the cells potential we increase the cells own ability to produce energy. Cheng does not exclude the contribution of other factors but states this is the mechanism of action he observed as a major factor.

Footnotes

1. Lehninger, Albert L. , Principles of Biochemistry. New York, N.Y: Worth Publishers, Inc, 1982.

2. Ibid.

3. Darnell, James, and Harvey Lodish, and David Baltimore, Molecular Cell Biology. New York, N.Y: Scientific American Books, 1986.

4. Purves, William K. and Gordian H. Orians, Life: The Science of Biology, Sinauer Ass., Sunderland, Mass. 1983.

5. Op. cit. Lehninger (1982) p.362.

6. Op. cit. Darnell (1986) p.626.

7. Ibid. p.627.

8. Schmidt, Robert, Ed. Fundementals of Neurophysiology, Springer Verlag, 1978. p.25, 42.

9. Jewewtt, L., et. al., Basic Concepts of Neuronal Function, Little, Brown, and Co., Boston, Mass. 1984. p.100.

10. Waters, Robert L. , et. al. Functional Electrical Stimulation. Downey, Ca.: Professional Staff Ass. , 1981. p. 13.

11. Ibid. p. 13.

12. Op. cit. Schmidt (1978) p.10.

13. Op. cit. Darnell (1986) pp. 715-42.

14. Op. cit. Jewett (1984).

15. Op. cit. Darnell (1986) pp. 715-42.

16. Luttgens, Kathryne, and Katherine F. Wells, Kinesiology. New York, N.Y: Saunders College Publishing, 1982. p. 58.

17. Barr, Murry L. The Human Nervous System. Harper and Row, 1974.

18. Op. cit. Darnell (1986) p. 714.

19. Travell, Janet G. , and David G. Simons, Myofascial Pain and Dysfunction: The Trigger Point Manual, Williams and Wilkins, Baltimore/London, 1983. p. 32.

20. Op. cit. Luttgens (1982) p. 33.

21. Op. cit. Darnell (1986) p.823.

22. Ibid. p.825.

23. Ibid. p.864.

24. Hudlicka, O. , et. al. (1977). The effects of long-term stimulation of fast muscles on their blood flow and metabolism. *Pftugers Arch.* 369. 141-149.

25. Op. cit. Travell (1983).

26. Wing, Thomas W. (1984) Trigger point therapy. *Digest of Chiro. Econ.* 78-81. March/April.

27. Ibid.

28. Op. cit. Jewett. p. 161.1.

29. Guyton, Arther C. Medical Text, W.B. Saunders: Phila. (1976). p. 72.

30. Ibid. p. 69.

31. Op. cit. Darnell (1986) p. 673.

32. Nelson, Roger M. , and Dean P. Currier, Clinical Electrotherapy. Norwalk, Connecticut: Appleton and Lange, 1987. p. 195.

33. Sears, Francis W. , University Physics. Reading, Massachusettes: Addison-Wesley Pub. Co. , 1982. pp. 460-469.

34. Personal quote, Peter H. Lathrop, Ph.D. Industrial Medical Center.

35. Op. cit. Waters (1981) p. 24.

36. Picker, Robert. (1987) Micro electrical neuromuscular stimulation. *The American Chiropracter.* Vol 1(2) 572-574.

37. Carley, Patrick J. and Stanley F. Warnapel. (1986) Electrotherapy for acceleration of wound healing: low intensity direct current. *Arch Phys Med Rehabil.* Vol. 66 443-446.

38. Op. cit. Picker (1987).

39. Becker, Robert O. (1974) Data transmission and control. *Annals New York Academy of Sciences*, Syracuse, N.Y.

40. Op. cit. Hudlika (1977).

41. Pette, Dirk, et. al. (1973) Effects of long-term stimulation of fast rabbit muscles. *Pflugers Arch.* 338: 257-272.

42. Cheng, Nook, et. al. (1982) Effects of electric currents on ATP generation in rat skin. *Clin Ortho and Rel Res.* Number 171, Nov.-Dec.

43. Patel, Nilesh and Mu-Ming Poo. (1982) Orientation of neurite growth by extracellular electric fields. *J. Neuroscience*, Vol 2. No 4, pp 483-496.

44. Pilla, Arthur A. (1974) Electrochemical information transfer. *Annals New York Academy of Sciences.* 138-167.

45. Barron, Jesse J. , et. al. (1985) Treatment of decubitus ulcers. *Minnesota Medicine.* (Feb) 103-106.

46. Forgen, M. et. al. (1985) Bone growth accelerated by stimulation of the epiphyseal plate with electric current. *Arch Ortho Trama Surg.* 104: 121-124.

47. Op. cit. Cheng (1982).

48. Ibid.

49. Wall, Patrick, and Ronald Melzack, Textbook of Pain. New York, N.Y: Churchill Livingstone, 1984. p. 146.

50. Op. cit. Guyton. p. 72.

51. Op. cit. Wall (1984) pp. 681-689.

52. Ibid.

53. Op. cit. Wing (1984).

54. Becker, Robert O. The Body Electric, William Morrow Inc., New York, N.Y. 1985. p. 259 .

55. Ibid.

56. Wolbarsht, M.L. , Ed. Laser Applications in Medicine and Biology. Plenum Press, N.Y. Vol. 3, 1977. [Reprints from: A Summary of Research in Biostimulation]

57. Ibid. Becker (1974).

58. Royal, F. Fuller, and Craig K. Mayfield. Physicians Electro Diagnostic Handbook, Nevada Clinic of Preventive Medicine. L.V. Nevada. p. 162.

59. Bogatyryov, Vladenir. Soviet Life. " Treating Diseases Without Drugs. " No. 3, (258), March 1978. [Reprints from: A Summary of Research in Biostimulation]

60. Op. cit. Royal p. 161.

61. Op. cit. Bogatyryov (1978).

62. Op. cit. Pilla (1974).

63. Op. cit. Becker (1985).

64. Cochran, G.V.B. et. al. (1985) Piezo electric internal fixation devices: a new approach to electrical augmentation of osteogenisis. J. *Orthopedic Res.* 3: 508-513.

65. Black, Jonathon. (1984) Tissue response to exogenous electromagnetic signals. *Orthopedic Clinics of North America.* Vol. 15. No 1.

66. Op. cit. Becker (1985).

67. Op. cit. Forgen (1985).

68. Op. cit. Cheng (1982).

69. Op. cit. Darnell (1986) p. 875.

70. Ibid. p. 875

71. Op. cit. Sears (1982)

72. Op. cit. Cheng (1982).

73. Op. cit. Jewett (1984).

74. Op. cit. Wall (1984) p. 6.

75. Op. cit. Becker (1985) p. 206.

76. Ibid. p. 206.

77. Op. cit. Patel (1982).

78. Robinson, K.R. and R.F. Stump. (1984) Self-generated electrical current through *Xenopus* neuralae. *J. Physiol.* 352: 339-352.

79. McCaig, Colin D. (1986) Electric fields, contact guidance and the direction of nerve growth. *J. Embryol. exp. Morph.* 94:245-255.

80. Borgens, Richard B. (1986) Transsected dorsal column axons within the guinea pig spinal cord regenerate in applied electric field. *J. Comp. Neur.* 250: 168-180.

81. Op. cit. Robinson (1984). p. 344.

82. Freeman, J.A., et. al. (1985) Steady growth cone currents. *J. Neur. Res.* 13: 257-283.

83. Borgens, Richard B. (1986) Roll of natural and applied electric fields in neuronal regeneration. *Ionic Currents.* Allen R. Liss, Inc. 239-250.

84. Op. cit. Becker (1974).

85. Ibid.

86. Ibid.

87. Ibid.

88. Kenyon, Julian M. (1979) Bioelectric potentials and their relation to acupuncturo. *Acupuncturo and Electro-Therapeut. Res, Int. J.* 4: 37-41.

89. Kroetlinger, Michael. (1980) On the use of the laser in acupuncture. *Acupuncture and Electro-Therapeutics Res. , Int. J.* , Vol. 5, pp 297-311.

90. Op. cit. Becker (1974).